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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/005,675	11/07/2001	Steven Shak	P0530P1C10	1479

9157 7590 12/04/2003

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EXAMINER	
WITZ, JEAN C	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 12/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

SM

Office Action Summary	Application No.	Applicant(s)	
	10/005,675	SHAK, STEVEN	
	Examiner	Art Unit	
	Jean C. Witz	1651	

-- The MAILING DATE of this communication appears on the cover sh et with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28,29 and 35-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28,29 and 35-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Pri rity under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 28-29 and 35-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over the teachings of Lieberman, Cliffton et al., Segal et al., and Salomon et al. taken as a whole and combined with Funakoshi et al., Ito et al. and Khouw et al., optionally in view of Suggs et al.

The claims are drawn to methods of 1) treating a patient having an accumulation of purulent material, 2) enhancing the activity of antibiotics, 3) treating a patient having cystic fibrosis, 5) treating a patient having bronchitis and 5) treating a patient having bronchiectasis all comprising the administration of a therapeutically effective amount of human Dnase free of proteases.

Lieberman teaches that DNA present in mucopurulent secretions of individuals suffering from respiratory diseases contribute to the chronicity of the diseases because the DNA increases the viscosity of the secretions. The reference further teaches that "a therapeutic attack upon the DNA content of purulent respiratory secretions would therefore appear to be worthwhile in an attempt to reduce morbidity from respiratory infection and to enhance the effectieness of antibiotics." The reference teaches that pancreatic dornase, an enzyme preparation containing Dnase along with amounts of

chymotrypsin and trypsin, was effective in reducing the viscosity of mucopurulent secretions of patients suffering from cystic fibrosis, allowing them to more easily clear the secretions from bronchi and lungs.

Cliffton et al., similarly successfully uses pancreatic dornase in the treatment of brochiectasis, bronchitis and other chronic pulmonary diseases where the enzyme composition breaks down the viscous mucopurulent secretions blocking the bronchi, allowing the mucopurulent secretions to be more easily cleared.

Segal et al. evaluated pancreatic dornase as a treatment of mucopurulent secretions in the tracheobronchial tree and found it to be effective in the therapy of "bronchopulmonary disease in which tenacious mucopurulent secretions constitute a major factor in the pathological process, and in which evacuation of the secretions is of utmost importance."

Salomon et al. treated patients suffering from bronchiectasis, bronchitis and other chronic pulmonary diseases with pancreatic dornase and noted beneficial effects in virtually all patients.

The references differ from the claims in that the Dnase is of bovin origin and that the administered composition contains proteases.

Funakoshi et al. discloses the isolation and purification of human Dnase I from the pancreas and discloses at page 1776 that "the preparation obtained was free from other nucleolytic or proteolytic enzymes."

Ito et al. discloses the purification of human Dnase I from urine which was immunologically identical to human pancreatic Dnase I.

The references differ from the claims in that they do not distinctly disclose the use of purified human Dnase in the treatment of bronchopulmonary diseases characterized by mucopurulent secretions.

Khouw et al. disclose highly purified Dnase free of impurities and proteases. The reference states that Dnase is known to have several medical therapeutic uses, such as to "liquefy pus". Khouw et al. states that Dnase is found in the pancreas, blood and spleen and animals and suggests bovine pancreas or spleen or porcine pancreas as a common source of Dnase.

Suggs et al. teach the use of mixtures of chemically synthesized oligodeoxyribonucleotides as hybridization probes for the isolation of specific cloned DNA sequences. The approach is to "chemically synthesize a mixture of oligonucleotides that represent all possible codon combinations for a small portion of the amino acid sequence of a given protein." Once a protein, in this case, Dnase, is purified, amino acid sequencing can be performed by any of the techniques well known and used in the art, such as the dideoxy method of Sanger et al., or modern automated Edmand degradation. Under the principle that one sequence must be complementary to the DNA for that protein, "the complementary oligonucleotide will form a perfectly base paired duplex with the DNA from the coding region . . . ." Thus, mixed oligonucleotide probes allow the isolation of DNA sequences for any protein with a known portion of the amino acid sequence.

The prior art also teaches that at the time of the invention was made, purified human Dnase I was available from both natural sources and as a result of synthetic

administration of heterologous proteins run the risk of immune sensitization, and while such was not reported in the prior art cited, it is axiomatic within the protein pharmaceutical art that whenever possible, it is always preferable to administer a homologous protein in its most pure form.

Therefore, it would have been obvious to one of ordinary skill in the art to use human Dnase free of proteases in an old and conventional treatment of bronchopulmonary conditions associated with mucopurulent material with the therapeutic benefits both as described in the prior art and expected as a result of the use of a purer, homologous therapeutic formulation.

Conclusion

This is a continuation-in-part of applicant's earlier Application No. 09/669,306. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jean C. Witz whose telephone number is (703) 308-3073. The examiner can normally be reached on 6:30 a.m. to 4:00 p.m. M-Th and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on (703) 308-4743. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Jean C. Witz
Primary Examiner
Art Unit 1651